Omalizumab (XOLAIR) Criteria for Use in Asthma

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

Exclusion Criteria (if ONE is checked, patient is not eligible)

- ❑ Prior allergic reaction to omalizumab
- ❑ Do not use to treat acute exacerbation of asthma or status asthmaticus

Inclusion Criteria

The following 8 criteria must be met:

- ❑ Provider is a pulmonologist or allergy specialist
- ❑ Moderate-severe persistent asthma
- ❑ Pre-treatment serum IgE 30-700 IU/ml[1]
- ❑ Positive skin tests or *in vitro* reactivity to common aeroallergen (e.g. dust mites, pet dander, and cockroach
- ❑ Symptomatic or has exacerbations despite having received optimal therapy for their asthma (e.g. medium-high dose inhaled corticosteroid and long-acting beta2-agonist)
- ❑ Adherent to medications as evidenced by a review of prescription refill history during the last 12 months
- ❑ Patient should be nonsmoking and if not, actively receiving smoking cessation treatment[2]
- ❑ Patient has an epinephrine pen

[1] Data for use in patients with baseline IgE serum levels up to 1500 IU/mL are available (considered off-label in the US). Use of omalizumab in such patients should be adjudicated locally.

[2] There is limited information on the efficacy and safety of omalizumab in patients who smoke. The decision to use omalizumab in patients who have had unsuccessful attempts at smoking cessation should be made on a case-by-case basis.

Dosage and Administration

Please refer to Product Information for detailed information on preparation, dosage, and administration

Note: Administer omalizumab in a healthcare setting. Omalizumab is administered subcutaneously, Dose and dosing frequency is based on serum total IgE level measured before the start of treatment and body weight. No more than 150mg is injected at a single site. Doses > 150mg are to be divided among more than 1 injection site.

Monitoring

Effectiveness of therapy should be evaluated within 3-6 months and discontinued if not useful. Goal should be the objective improvement in selected markers of asthma control, such as symptoms severity, frequency of rescue treatments, oral steroid requirements, and frequency of urgent outpatient visits and/or hospitalization.

Issues for Consideration

- Give patient the omalizumab Medication Guide and instruct them to read it before each dose of omalizumab
- Risk of anaphylaxis (please refer to the product package insert for detailed information)
    - In clinical trials, the occurrence was 0.14% (omalizumab) and 0.07% (control). In post-marketing safety database between 6/1/03 and 12/31/06, there were 120 cases of possible anaphylaxis with omalizumab reported (equals to a rate of 2 per 1000 patients treated based on an estimated exposure of 57,300 patients)
    - Educate patient on signs and symptoms of severe hypersensitivity and anaphylaxis
    - Patients should carry and know how to initiate emergency self-treatment for anaphylaxis
    - Observe patients for an appropriate amount of time after each injection (e.g., in clinical trials, patients were observed for 2 hours after the 1st dose and 1 hour for subsequent doses).
    - Healthcare professionals should be prepared to manage life-threatening anaphylaxis
    - If a severe hypersensitivity reaction occurs, omalizumab should be discontinued
    - Anaphylaxis can occur after any dose even if previous doses were well tolerated (39% of reported cases occurred

after the first dose)
    - According to post-marketing data, a prior history of anaphylaxis unrelated to omalizumab was reported in 24% of cases of anaphylaxis to omalizumab

- Patients receiving omalizumab and traveling to endemic parasitic regions should be monitored for such infections. A one-year study conducted in Brazil found that 53% of patients receiving omalizumab developed an infection compared to 42% of placebo controls (OR 1.96 [95%CI 0.88, 4.36]).

- It is unknown if IgE plays a surveillance role in cancer prevention and whether blocking IgE is associated with an increase in cancer incidence. In the clinical trials, the incidence of new or recurrent cancer with omalizumab and placebo was 0.5% and 0.2% respectively. The majority of these patients were observed for less than 1year. When expressed as 1000 patient-years of exposure the event rate was 6.3 and 3.3 respectively.

  More recently, a pooled analysis of all clinical trials and EXCELS, a FDA-required Phase 4 safety study (prospective observational cohort) indicate no increased risk of malignancy. In the EXCELS trial (mean follow-up 3.7 years), the rate of primary malignancy was 12.3 and 13.0 per 1000 patient/years respectively for omalizumab and non-omalizumab patients. In EXCELS, 5% of patients were current smokers and 29% past smokers. However, there were several study limitations which prevent from definitively ruling out a malignancy risk. Study limitations include unmeasured/uncontrolled confounding, exclusion of patients with history of cancer or a premalignant condition, high study discontinuation rate (46% omalizumab; 40% non-omalizumab), and the bias introduced by allowing enrollment of patients previously exposed to omalizumab (88%).

- In the EXCELS observational trial the incidence rate for overall cardiovascular and cerebrovascular serious adverse events (SAEs) were 13.4 and 8.1 per 1000 patient-years respectively for omalizumab and non-omalizumab groups. The results suggest a potential increased risk of serious cardiovascular and cerebrovascular events in patients treated with omalizumab; however, there were several limitations noted in the study including imbalances in baseline cardiovascular risk factors between groups and others as described under the malignancy discussion which limit the ability to quantify the magnitude of risk (refer to the product package insert for more detailed information).